

**Human Sel-10 Polypeptides and Polynucleotides that Encode Them****CROSS-REFERENCE TO RELATED APPLICATIONS**

This application claims the benefit of the following provisional application: U.S. Serial No. 60/068,243, now abandoned, filed 19 December 1997, under 35 USC 119(e)(1). This application also claims the benefit of the following application: U.S. Serial No. 09/213,888, filed 17 December 1998, under 35 USC 120.

**FIELD OF THE INVENTION**

The present invention provides isolated nucleic acid molecules comprising a polynucleotide encoding either of two alternative splice variants of human sel-10, one of which is expressed in hippocampal cells, and one of which is expressed in mammary cells. The invention also provides isolated sel-10 polypeptides.

**BACKGROUND OF THE INVENTION**

Alzheimer's disease (AD) is a degenerative disorder of the central nervous system which causes progressive memory and cognitive decline during mid to late adult life. The disease is accompanied by a wide range of neuropathologic features including extracellular amyloid plaques and intra-neuronal neurofibrillary tangles. (Sherrington, R., *et al.*; *Nature* 375: 754-60 (1995)). Although the pathogenic pathway leading to AD is not well understood, several genetic loci are known to be involved in the development of the disease.

Genes associated with early onset Alzheimer's disease (AD) have been identified by the use of mapping studies in families with early-onset AD. These studies have shown that genetic loci on chromosomes 1 and 14 were likely to be involved in AD. Positional cloning of the chromosome 14 locus identified a novel mutant gene encoding an eight-transmembrane domain protein which subsequently was named presenilin-1 (PS-1). (Sherrington, R., *et al.*; *Nature* 375: 754-60 (1995)). Blast search of the human EST database revealed a single EST exhibiting homology to PS-1, designated presenilin-2 (PS-2) which was shown to be the gene associated with AD on chromosome 1. (Levy-Lahad, E. *et al.*, *Science* 269:973-977 (1995); Rogaev, E. I., *et al.*, *Nature* 376: 775-8 (1995); Li, J. *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* 92: 12180-12184 (1995)).